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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,865	11/20/2003	Nobuya Matsuoka	245748US0CONT	5646

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1609	

NOTIFICATION DATE	DELIVERY MODE
09/21/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/716,865	MATSUOKA ET AL.	
	Examiner	Art Unit	
	Samira Jean-Louis	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-48* is/are pending in the application.

4a) Of the above claim(s) *37,38 and 45-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/926469.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *Sheets (2)*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *08/27/07)*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse to various groups and species in the reply filed on 08/28/07 is acknowledged. The traversal is on the ground(s) that the search of all the species does not impose an undue burden upon the examiner. This is not found persuasive because the claims recited in the instant application recite a multiplicity of species of active compounds that are different in chemical structure and would therefore acquire separate status in the art (i.e. different classification). For example, the application recite both barbiturates and a flavones as antagonistic compounds for the adenosine A_1A_{2a}-receptor. Specifically, barbiturates are classified under 544, subclass 300 while flavones are classified in 536, subclass 8. Thus, in this instance, these species are patentably distinct and fully capable of supporting separate patents. Furthermore, given that the claims recite such a multiplicity of species, the search would indeed be unduly extensive and burdensome given that a search for these species would consist of searching multiple databases for various references and literature searches.

Thus, the requirement is still deemed proper and is therefore made FINAL.

Claims 37-38, and 45-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group and species, there being no allowable generic or linking claim.

Claims 37-48 are pending in the instant application; however, as a result of the restriction requirement and election of species, claims 39-44 are being examined on the merits herein.

Response to Arguments

Applicant's arguments filed on August 10, 2006 with regards to the *scope of enablement rejection* under *35 U.S.C. 112, first paragraph* of the claims over the prior art have been fully considered but they are not found persuasive.

Claims 39-44 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating catalepsy (in mice), improving impaired-memory (in male SD rats), and anti-anxiety (in Wistar rats), with the antagonist 3-[2-(thiazole-2-ylmethyl)-3-oxo-2,3-dihydro-pyridizin-6-yl], does not reasonably provide enablement for treating Parkinson's disease and the prevention and/or treatment of the concomitant symptoms thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In particular, Applicants' argue that claims 39-48 which are directed to a method of using compounds having dual A_1A_{2a}-receptor antagonistic activity is enabled for a method of use given the supportive animal data provided in the specification. This argument is not found to be persuasive for the previous reasons suggested in the rejection on 02/10/06.

In addition, though applicant provided some working examples, no convincing data was provided as to enable one skilled in the art to treat Parkinson disease with these compounds. As previously indicated in the previous rejection, applicant is enabled for treating catalepsy (in mice), improving impaired-memory (in male SD rats), and anti-anxiety (in Wistar rats), with the antagonist 3-[2-(thiazole-2-ylmethyl)-3-oxo-2,3-dihydro-pyridizin-6-yl]; however, this does not reasonably provide enablement for treating Parkinson's disease and the prevention and/or treatment of the concomitant symptoms thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope.

Furthermore, while applicant exemplified the use of a specific dual A_1A_{2a}-receptor antagonistic compound in mice and/or rats, applicant did not provide sufficient statistical analyses in their results nor did applicant utilized any Parkinson animal models such as

the reserpine model, neuroleptic-induced catalepsy, tremor models, or an experimentally-induced degeneration mice of nigro-striatal dopaminergic neurons (see ***Gerlach et al. Animal models of Parkinson's disease: An empirical comparison with the phenomenology of the disease in man. (1996), Journal of Neural Transmission, Vol. 103, Issue 8-9, pgs. 987-1041***). Given that the animal models presented in the instant application do not commensurate to patients with Parkinson disease, one skilled in the art would not be enabled to practice the disclosed invention to treat and/or prevent Parkinson disease without undue experimentation.

Regarding the "*prevention of Parkinson disease*", the Examiner notes that the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing Parkinson's disease given that no laboratory tests is in existence for the diagnosis of the disease. Moreover, the specification does not provide any guidance as to a specific method to be used in order to show the effectiveness of the aforementioned compound for preventing Parkinson disease. Consequently, for the reasons cited above and the previous rejection, the Examiner maintains the rejection under *35 U.S.C. 112, first paragraph*.

The rejection of claims 19-38 under 35 U.S.C. 102 (b) as being anticipated by Akahane et al. (WO 98/03507) is being withdrawn in view of Applicants arguments and remarks. In particular, the Examiner agrees that **Akahane** does not specifically disclose the use of the antagonist 3-[2-(thiazole-2-ylmethyl)-3-oxo-2,3-dihydro-pyridizin-6-yl]

solely for the treatment of Parkinson's disease and thus would not be anticipated by Akahane.

The claims are being newly rejected as follows.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 39-44 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Akahane et al. (WO 98/03507) in view of Popoli et al. (Neurosciences Letters, 1998, pg. 201-204) and in further view of Meara (Age and Ageing, 1994, pg. 1-8).

Akahane et al. teaches the use of the aforementioned compound as a pharmaceutical composition for the treatment of Parkinson's disease (see abstract, claims 1-9, 12, and 14, pgs. 73-86). Specifically, this method of treatment further provides for a pharmaceutical composition of the antagonist 3-[2-(thiazole-2-ylmethyl)-3-oxo-2,3-dihydro-pyridizin-6-yl] for the treatment of various diseases including Parkinson diseases (see claim 12, page 84). Moreover, the specific compound to be treated is taught by Akahane and meets the requirements of the elected compound (instant claim

44 vs. pgs. 9-10 regarding compound If). Furthermore, Akahane teaches that the aforementioned compound of formula (I) are adenosine antagonists (abstract, claim 14).

Akahane et al. does not specifically teach a method of treating only Parkinson disease with the compound of formula (If)

Popoli teaches that the dual A_1A_{2a}-receptor plays a role in the control of motor ability. Specifically, the work of Popoli et al. indicated that the blockade of both receptor subtypes is involved in motor activity in Wistar rats (see abstract).

Meara further teaches that Parkinson disease is characterized by motor abnormalities. Specifically, Meara discloses that several motor signs impairments exists in Parkinson ranging from bradykinesia, akinesia to tremor and rigidity (see page 2, 2nd paragraph).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to combine the method of Akahane with the knowledge of the dual A_1A_{2a}-receptor antagonistic provided by Popoli and the knowledge of motor impairment provided by Meara to treat motor impairment (a symptom characterized by Parkinson disease) and also arrive at the method of applicant since Akahane in view of Popoli essentially teaches a method of treating Parkinson disease using the pharmaceutical compound of formula (If) composition disclosed by Akahane. Given that Akahane

teaches a method of treating Parkinson disease using the antagonist 3-[2-(thiazole-2-ylmethyl)-3-oxo-2,3-dihydro-pyridizin-6-yl] and Popoli discloses that targeting the A_1A_{2a}-receptor will stimulate motor activity (found deficient in Parkinson disease), one of ordinary skill would have been motivated to combine the method of Akahane et al. with the disclosure of Popoli with the expectation of treating Parkinson disease and the concomitant symptoms such as motor impairment.

Though Akahane did not teach the binding affinity of the aforementioned compound of A1 in relation to the A2a receptor, it is considered that one of ordinary skill in the art at the time of the invention was made would found it obvious to conclude that the compound of formula (If) disclosed by Akahane would possess the same binding affinity as that disclosed by the applicant given that these characteristics are an inherent property of the compound and confers no patentable weight.

It is noted that In re Best,195 USPQ 430, and In re Fitzgerald, 205 USPQ 594, discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Conclusion

Claims are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-5 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ardin H. Marschel 9/17/07

SJL

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

09/13/2007